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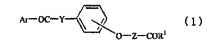
(54) [Title of the invention] A hypoglycaemic agent.

(57) [**Abstract**]

[Solution] A hypoglycaemic agent which has as its active ingredient an arylamide derivative as expressed by the following General Formula (1)

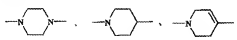
[*Form. 1*]



(1)

[in which Ar indicates a phenyl group, naphthyl group, pyridinyl group, furyl group, thienyl group, quinolyl group or indolyl group, which may have a substituent group; Y indicates the group

[*Form. 2*]



(a) (b) (c)

or

(d)

Z indicates an alkylene group with a carbon number of 1~5 and a straight chain or branched chain; and R^1 indicates a hydroxyl group, alkoxy group or $-NH(CH_2)_mCOOH$ (where m is a number in the range 1~3)]

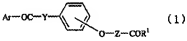
or a salt thereof.

[Effects] Since the hypoglycaemic agent according to the present invention has excellent hypoglycaemic actions, it can be used for the prevention or treatment of diabetes mellitus or obesity and, in particular, for the prevention of the onset or progress of atherosclerosis in diabetes mellitus with complicating lipid metabolisms abnormality and is of great clinical utility.

[**Claims**]

[Claim 1] A hypoglycaemic agent which has as its active ingredient an arylamide derivative as expressed by the following General Formula (1)

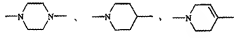
[*Form. 1*]



(1)

[in which Ar indicates a phenyl group, naphthyl group, pyridinyl group, furyl group, thienyl group, quinolyl group or indolyl group, which may have a substituent group; Y indicates the group

[*Form. 2*]



(a) (b) (c)

or

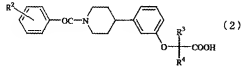
(d)

Z indicates an alkylene group with a carbon number of 1~5 and a straight chain or branched chain; and R^1 indicates a hydroxyl group, alkoxy group or $-NH(CH_2)_mCOOH$ (where m is a number in the range 1~3)]

or a salt thereof.

[Claim 2] A hypoglycaemic agent according to Claim 1, in which the arylamide derivative is a compound expressed by the following General Formula (2)

[*Form. 3*]



(2)

[in which R^2 indicates a halogen atom; R^3 and R^4, which may be the same or different, indicate a hydrogen atom or methyl group].

[Claim 3] A hypoglycaemic agent according to Claim 1, in which the arylamide derivative is 2-[3-[1-(4-fluorobenzoyl)piperidin-4-yl]phenoxy]-2-methyl propionic acid.

[Detailed Description of the Invention]

[0001]

[Technical field] The present invention relates to a hypoglycaemic agent which has as its active ingredient an arylamide derivative or a salt of this.

[0002]

[Prior art] With the increasing adoption of Western dietary habits and an ageing population, diabetes mellitus (insulin non-dependent diabetes mellitus: NIDDM), a disease caused by lowered insulin resistance of the target tissue of insulin or inadequate insulin secretion by pancreatic ß cells, has shown a steady increase in incidence.

[0003] Therapeutic agents for NIDDM have principally been sulphonyl urea drugs which improve insulin undersecretion but recently attention has focused on the importance of insulin resistance for the onset of NIDDM and drugs have been developed that show hypoglycaemic activity not by stimulating insulin secretion but by reducing the insulin resistance of the insulin target tissues and these compounds have included thiazolidine derivatives such as troglytazone and pioglytazone and thiazolidine derivatives with a bicyclic lactam structure or cyclic urethane structure (JP 6-157522 (A), JP 6-502144 (B) etc).

[0004] However, sulphonyl urea drugs often cause severe hypoglycaemia and the compounds that lower insulin resistance are inadequate in their hypoglycaemic effects and their ability to inhibit diabetes complications such as hyperlipidaemia.

[0005]

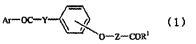
[Problems the invention aims to solve] The object of the present invention is to propose a hypoglycaemic agent which is both safe and has excellent hypoglycaemic actions and is useful in the treatment and prevention of diabetes mellitus and obesity.

[0006]

[Means by which the problems are solved] With this problem in mind, the present inventors examined a range of compounds and, unexpectedly, discovered that arylamide derivatives that have blood cholesterol lowering action and blood triglyceride lowering actions and are of utility as anti-hyperlipidaemia agents (JP 2952551 (B)) also have excellent hypoglycaemic actions and also discovered that these could be preventative and therapeutic agents for diabetes mellitus and obesity and the present invention was completed on the basis of this discovery.

[0007] Thus the present invention proposes a hypoglycaemic agent which has as its active ingredient an arylamide derivative as expressed by the following General Formula (1)

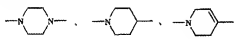
[*Form. 4*]



(1)

[in which Ar indicates a phenyl group, naphthyl group, pyridinyl group, furyl group, thienyl group, quinolyl group or indolyl group, which may have a substituent group; Y indicates the group

[*Form. 5*]



(a) (b) (c)

or

(d)

Z indicates an alkylene group with a carbon number of 1~5 and a straight chain or branched chain; and R^1 indicates a hydroxyl group, alkoxy group or $-NH(CH_2)_mCOOH$ (where m is a number in the range 1~3)]

or a salt thereof.

[0008]

[Preferable embodiments of the invention] In General Formula (1), Ar indicates a phenyl group, naphthyl group, pyridinyl group, furyl group, thienyl group, quinolyl group or indolyl group, which may have a substituent group, and the phenyl group which may have a substitutent group means, apart from a phenyl group, a phenyl group substituted with 1~3 of halogen atom, hydroxyl group, alkyl group, haloalkyl group, alkoxy group, alkenyl group, acylamino group or carboxyalkyloxy group for example.

[0009] Here, the alkyl group should preferably be linear or branched and have a carbon number in the range 1~6; specifically, this may be, for example, methyl group, ethyl group, n-propyl group, i-propyl group, n-butyl group, i-butyl group, t-butyl group, n-pentyl group, i-pentyl group or n-hexyl group.

[0010] The halogen atom may be, for example, a fluorine atom, chlorine atom, bromine atom, or iodine atom. Of these, fluorine atom and bromine atom are preferable.

[0011] The haloalkyl group should preferably be linear or branched, have a carbon number of 1~6 and have 1~3 substituted halogen atoms; specifically, this may be, for example, a trifluoromethyl group or 1,1,1-trifluoroethyl group.

[0012] The alkoxy group should be, preferably, linear or branched and have a carbon number of 1~6; specifically, it may be, for example, a methoxy group, ethoxy group, n-propyloxy group, i-propyloxy group, n-butyloxy group, i-butyloxy group, t-butyloxy group, n-pentyloxy group, i-pentyloxy group or n-hexyloxy group.

[0013] The alkenyl group should preferably have a carbon number of 2~6; it may be, for example, a vinyl group, propenyl group, allyl group, butenyl group or pentenyl group.

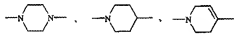
[0014] The acylamino group should preferably be an alkanoylamino group with a carbon number of 2~6; it may be, for example, a formylamino group, acetamino group, propionylamino group or butyrylamino group. The alkylene group with a carbon number of 1~3 may be, for example, a methylene group, ethylene group or propylene group.

[0015] The carboxyalkyloxy group should preferably be a carboxyalkyloxy group with a total carbon number of 2~7; it may be, for example, a carboxymethyloxy group, carboxyethyloxy group or carboxypropyloxy group.

[0016] The Ar is preferable when it is a phenyl group which may have substituent group, and, of these, a phenyl group which may have one or two substitutions with halogen atoms, is preferable and a phenyl group which may have one or two substituted fluorine atoms is particularly preferable.

[0017] Y indicates a cyclic amino group chosen from (a)~(d) below:

[*Form. 6*]



(a) (b) (c)

or

(d)

and, of these, a case when this is (b) piperidin-4-yl is particularly preferable.

[0018] The linear or branched alkylene group with a carbon number of 1~5 indicated by Z may be, for example, methylene, ethylene, propylene or other linear alkylene group or -$CH(CH_3)$-, -$C(CH_3)_2$-, -$C(C_2H_5)_2$- or other branched alkylene group and the branched alkylene group -$C(CH_3)_2$- is particularly preferable.

[0019] The salt of the arylamide derivative (1) according to the invention is not particularly limited provided that it is a pharmacologically permissible salt; it may be, for example, an alkali metal salt, inorganic salt or organic salt. More specifically, the alkali metal salt may be, for example, a lithium salt, sodium salt, potassium salt or magnesium salt; the inorganic salt may be, for example, hydrochloric acid salt, sulphuric acid salt, nitric acid salt, hydrobromic acid salt or phosphoric acid salt; and the organic salt may be, for example, an acetic acid salt, oxalic acid salt, citric acid salt, malic acid salt, fumaric acid salt, maleic acid salt, succinic acid salt, butyric acid salt, tartaric acid salt, methanesulphonic acid salt, benzenesulphonic acid salt or p-toluenesulphonic acid salt.

[0020] Specific examples of the arylamide derivative (1) according to the invention. are given below. 2-(1-benzoylpiperidin-4-yl) α, α-dimethylphenoxyacetic acid, 4-(1-benzoylpiperidin-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-benzoylpiperidin-4-yl) α, α-dimethylphenoxyacetic acid isopropyl, 2-{1-(4-methylbenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 4-{1-(4-methylbenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-methylbenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid isopropyl, 2-{1-(4-methoxybenzoyl) piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-methoxybenzoyl) piperidine-4-yl} α, α-dimethylphenoxyacetic acid (i.e. 2-[3-[1-(4-methoxybenzoyl) piperidin-4-yl]phenoxy]-2-methylpropionic acid), 4-{1-(4-methoxybenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-methoxybenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid isopropyl,

[0021] 2-{1-(4-fluorobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-fluorobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid (i.e. 2-[3-[1-(4-fluorobenzoyl)piperidin-4-yl]phenoxy]-2-methylpropionic acid), 4-{1-(4-fluorobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-fluorobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid isopropyl (i.e. 2-[3-[1-(4-fluorobenzoyl)piperidin-4-yl]phenoxy]-2-methylpropionic acid isopropyl), 2-{1-(4-chlorobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-chlorobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid (i.e. 2-[3-[1-(4-chlorobenzoyl)piperidin-4-yl]phenoxy]-2-methylpropionic acid), 4-{1-(4-chlorobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-chlorobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid isopropyl, 2-{1-(4-bromobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 4-{1-(4-bromobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid,

[0022] 2-{1-(4-iodobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-iodobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid (i.e. 2-[3-[1-(4-iodobenzoyl) piperidin-4-yl] phenoxy]-2-methylpropionic acid), 4-{1-(4-iodobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-iodobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid isopropyl, 2-{1-(4-

trifluoromethylbenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-trifluoromethylbenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid (i.e. 2-[3-[1-(4-trifluoromethylbenzoyl)piperidin-4-yl]phenoxy]-2-methylpropionic acid), 4-{1-(4-trifluoromethylbenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-trifluoromethylbenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid isopropyl, 2-{1-(4-hydroxy-3,5-iodobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-hydroxy-3,5-iodobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 4-{1-(4-hydroxy-3,5-iodobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-hydroxy-3,5-iodobenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid isopropyl,

[0023] 2-{1-(3, 5-di-t-butyl-4-hydroxybenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(3, 5-di-t-butyl-4-hydroxybenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid (i.e. 2-[3-[1-(3,5-di-t-butyl-4-hydroxybenzoyl)piperidin-4-yl]phenoxy]-2-methylpropionic acid), 4-{1-(3, 5-di-t-butyl-4-hydroxybenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(3, 5-di-t-butyl-4-hydroxybenzoyl)piperidin-4-yl} α, α-dimethylphenoxyacetic acid isopropyl, 2-(1-nicotinoylpiperidin-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-nicotinoylpiperidin-4-yl) α, α-dimethylphenoxyacetic acid (i.e. 2-[3-[1-(nicotinoyl)piperidin-4-yl]phenoxy]-2-methylpropionic acid), 4-(1-nicotinoylpiperidin-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-nicotinoylpiperidin-4-yl) α, α-dimethylphenoxyacetic acid isopropyl, 2-(1-isonicotinoylpiperidin-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-isonicotinoylpiperidin-4-yl) α, α-dimethylphenoxyacetic acid, 4-(1-isonicotinoylpiperidin-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-isonicotinoylpiperidin-4-yl) α, α-dimethylphenoxyacetic acid isopropyl,

[0024] 2-(1-(2-furancarbonyl)piperidin-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-(2-furancarbonyl)piperidin-4-yl) α, α-dimethylphenoxyacetic acid, 4-(1-(2-furancarbonyl)piperidin-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-(2-furancarbonyl)piperidin-4-yl) α, α-dimethylphenoxyacetic acid isopropyl, 2-(1-(2-tenoyl)piperidin-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-(2-tenoyl)piperidin-4-yl) α, α-dimethylphenoxyacetic acid, 4-(1-(2-tenoyl)piperidin-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-(2-tenoyl)piperidin-4-yl) α, α-dimethylphenoxyacetic acid isopropyl, {2-(4-

benzoylpiperazinyl) phenoxy} α, α-dimethylacetic acid, {4-(4-benzoylpiperazinyl) phenoxy} α, α-dimethylacetic acid, {3-(4-benzoylpiperazinyl) phenoxy} α, α-dimethylacetic acid isopropyl,

[0025] [2-{4-(4-methylbenzoyl)piperazinyl}phenoxy] α, α-dimethylacetic acid, [4-{4-(4-methylbenzoyl)piperazinyl}phenoxy] α, α-dimethylacetic acid, [3-{4-(4-methylbenzoyl)piperazinyl}phenoxy] α, α-dimethylacetic acid isopropyl, [2-{4-(4-methoxybenzoyl)piperazinyl}phenoxy] α, α-dimethylacetic acid, [3-{4-(4-methoxybenzoyl)piperazinyl}phenoxy] α, α-dimethylacetic acid, [4-{4-(4-methoxybenzoyl)piperazinyl}phenoxy] α, α-dimethylacetic acid, [3-{4-(4-methoxybenzoyl)piperazinyl}phenoxy] α, α-dimethylacetic acid isopropyl, [2-{4-(4-fluorobenzoyl)piperazinyl}phenoxy] α, α-dimethylacetic acid, [3-{4-(4-fluorobenzoyl)piperazinyl}phenoxy] α, α-dimethylacetic acid, [4-{4-(4-fluorobenzoyl)piperazinyl}phenoxy] α, α-dimethylacetic acid, [3-{4-(4-fluorobenzoyl)piperazinyl}phenoxy] α, α-dimethylacetic acid isopropyl,

[0026] [2-{4-(2-tenoyl)piperazinyl}phenoxy] α, α-dimethylacetic acid, [3-{4-(2-tenoyl)piperazinyl}phenoxy] α, α-dimethylacetic acid, [4-{4-(2-tenoyl)piperazinyl} phenoxy] α, α-dimethylacetic acid, [3-{4-(2-tenoyl)piperazinyl}phenoxy] α, α-dimethylacetic acid isopropyl, 2-(1-benzoylpiperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-benzoylpiperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 4-(1-benzoylpiperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-benzoylpiperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid isopropyl, 2-{1-(4-methylbenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-{1-(4-methylbenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 4-{1-(4-methylbenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-{1-(4-methylbenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid isopropyl,

[0027] 2-{1-(4-methoxybenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-{1-(4-methoxybenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 4-{1-(4-methoxybenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-{1-(4-

methoxybenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid isopropyl, 2-{1-(4-fluorobenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-{1-(4-fluorobenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 4-{1-(4-fluorobenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-{1-(4-fluorobenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid isopropyl, 2-{1-(4-chlorobenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-{1-(4-chlorobenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 4-{1-(4-chlorobenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-{1-(4-chlorobenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid isopropyl,

[0028] 4-{1-(4-bromobenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 2-{1-(4-iodobenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-{1-(4-iodobenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 4-{1-(4-iodobenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-{1-(4-iodobenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid isopropyl, 2-{1-(4-trifluoromethylbenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-{1-(4-trifluoromethylbenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 4-{1-(4-trifluoromethylbenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-{1-(4-trifluoromethylbenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid isopropyl, 2-{1-(4-hydroxy-3,5-diiodobenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-{1-(4-hydroxy-3,5-diiodobenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 4-{1-(4-hydroxy-3,5-diiodobenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-{1-(4-hydroxy-3,5-diiodobenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid isopropyl,

[0029] 2-(1-(3,5-di-t-butyl-4-hydroxybenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-(3,5-di-t-butyl-4-hydroxybenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 4-(1-(3,5-di-t-butyl-4-hydroxybenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-(3,5-di-t-butyl-4-hydroxybenzoyl)piperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid isopropyl, 2-(1-nicotinoylpiperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-nicotinoylpiperidin-3-en-4-yl) α, α-

dimethylphenoxyacetic acid, 4-(1-nicotinoylpiperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-nicotinoylpiperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid isopropyl, 2-(1-isonicotinoylpiperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-isonicotinoylpiperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 4-(1-isonicotinoylpiperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-isonicotinoylpiperidin-3-en-4-yl) α, α-dimethylphenoxyacetic acid isopropyl,

[0030] 2-{1-(2-furancarbonyl)piperidin-3-en-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(2-furancarbonyl)piperidin-3-en-4-yl} α, α-dimethylphenoxyacetic acid, 4-{1-(2-furancarbonyl)piperidin-3-en-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(2-furancarbonyl)piperidin-3-en-4-yl} α, α-dimethylphenoxyacetic acid isopropyl, 2-{1-(2-tenoyl)piperidin-3-en-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(2-tenoyl)piperidin-3-en-4-yl} α, α-dimethylphenoxyacetic acid, 4-{1-(2-tenoyl)piperidin-3-en-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(2-tenoyl)piperidin-3-en-4-yl} α, α-dimethylphenoxyacetic acid isopropyl,

[0031] 2-{1-(4-methylbenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-methylbenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 4-{1-(4-methylbenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-methylbenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid isopropyl, 2-{1-(4-methoxybenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-methoxybenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 4-{1-(4-methoxybenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-methoxybenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid isopropyl,

[0032] 2-{1-(4-trifluoromethylbenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-trifluoromethylbenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 4-{1-(4-trifluoromethylbenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-trifluoromethylbenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid isopropyl, 2-{1-(4-hydroxy-3,5-

diiodobenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-hydroxy-3,5-diiodobenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 4-{1-(4-hydroxy-3,5-diiodobenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(4-hydroxy-3,5-diiodobenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid isopropyl,

[0033] 2-{1-(3,5-di-t-butyl-4-hydroxybenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(3,5-di-t-butyl-4-hydroxybenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 4-{1-(3,5-di-t-butyl-4-hydroxybenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(3,5-di-t-butyl-4-hydroxybenzoyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid isopropyl, 2-(1-isonicotinoyl-4-hydroxypiperidin-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-isonicotinoyl-4-hydroxypiperidin-4-yl) α, α-dimethylphenoxyacetic acid, 4-(1-isonicotinoyl-4-hydroxypiperidin-4-yl) α, α-dimethylphenoxyacetic acid, 3-(1-isonicotinoyl-4-hydroxypiperidin-4-yl) α, α-dimethylphenoxyacetic acid isopropyl,

[0034] 2-{1-(2-furancarbonyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(2-furancarbonyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 4-{1-(2-furancarbonyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(2-furancarbonyl)-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid isopropyl, 2-{1-(2-tenoyl)piperidin-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(2-tenoyl)piperidin-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 4-{1-(2-tenoyl)piperidin-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid, 3-{1-(2-tenoyl)piperidin-4-hydroxypiperidin-4-yl} α, α-dimethylphenoxyacetic acid isopropyl, 2-(4-benzoylpiperazinyl) ß-phenoxypropionic acid, 3-(4-benzoylpiperazinyl) ß-phenoxypropionic acid, 4-(4-benzoylpiperazinyl) ß-phenoxypropionic acid, 2-{4-(4-brombenzoyl)piperazinyl} ß-phenoxypropionic acid, 3-{4-(4-brombenzoyl)piperazinyl} ß-phenoxypropionic acid, 4-{4-(4-brombenzoyl)piperazinyl} ß-phenoxypropionic acid,

[0035] 2-(1-benzoylpiperidin-4-yl) ß-phenoxypropionic acid, 3-(1-benzoylpiperidin-4-yl) ß-phenoxypropionic acid, 4-(1-benzoylpiperidin-4-yl) ß-phenoxypropionic acid, 2-{1-(4-brombenzoyl)piperidin-4-yl} ß-phenoxypropionic acid, 3-{1-(4-brombenzoyl)piperidin-

4-yl} ß-phenoxypropionic acid, 4-{1-(4-brombenzoyl)piperidin-4-yl} ß-phenoxypropionic acid,

[0036] 2-(1-benzoylpiperidin-3-en-4-yl) ß-phenoxypropionic acid, 3-(1-benzoylpiperidin-3-en-4-yl) ß-phenoxypropionic acid, 4-(1-benzoylpiperidin-3-en-4-yl) ß-phenoxypropionic acid, 2-{1-(4-brombenzoyl)piperidin-3-en-4-yl} ß-phenoxypropionic acid, 3-{1-(4-brombenzoyl)piperidin-3-en-4-yl} ß-phenoxypropionic acid, 4-{1-(4-brombenzoyl)piperidin-3-en-4-yl} ß-phenoxypropionic acid,

[0037] 2-(1-benzoyl-4-hydroxypiperidin-4-yl) ß-phenoxypropionic acid, 3-(1-benzoyl-4-hydroxypiperidin-4-yl) ß-phenoxypropionic acid, 4-(1-benzoyl-4-hydroxypiperidin-4-yl) ß-phenoxypropionic acid, 2-{1-(4-brombenzoyl)-4-hydroxypiperidin-4-yl} ß-phenoxypropionic acid, 3-{1-(4-brombenzoyl)-4-hydroxypiperidin-4-yl} ß-phenoxypropionic acid, 4-{1-(4-brombenzoyl)-4-hydroxypiperidin-4-yl} ß-phenoxypropionic acid,

[0038] 2-{1-(1-naphthalenecarbonyl)piperidin-4-yl}phenoxyacetic acid, 2-{1-(1-naphthalenecarbonyl)piperidin-4-yl} ß-phenoxypropionic acid, 2-{1-(1-naphthalenecarbonyl)piperidin-4-yl} γ-phenoxybutyric acid, 3-{1-(1-naphthalenecarbonyl)piperidin-4-yl}phenoxyacetic acid, 3-{1-(1-naphthalenecarbonyl)piperidin-4-yl} ß-phenoxypropionic acid, 3-{1-(1-naphthalenecarbonyl)piperidin-4-yl} γ-phenoxybutyric acid, 4-{1-(1-naphthalenecarbonyl)piperidin-4-yl}phenoxyacetic acid, 4-{1-(1-naphthalenecarbonyl)piperidin-4-yl} ß-phenoxypropionic acid, 4-{1-(1-naphthalenecarbonyl)piperidin-4-yl} γ-phenoxybutyric acid,

[0039] 2-{1-(2-naphthalenecarbonyl)piperidin-4-yl}phenoxyacetic acid, 2-{1-(2-naphthalenecarbonyl)piperidin-4-yl} ß-phenoxypropionic acid, 2-{1-(2-naphthalenecarbonyl)piperidin-4-yl} γ-phenoxybutyric acid, 3-{1-(2-naphthalenecarbonyl)piperidin-4-yl}phenoxyacetic acid, 3-{1-(2-naphthalenecarbonyl)piperidin-4-yl} ß-phenoxypropionic acid, 3-{1-(2-naphthalenecarbonyl)piperidin-4-yl} γ-phenoxybutyric acid, 4-{1-(2-naphthalenecarbonyl)piperidin-4-yl} phenoxyacetic acid, 4-{1-(2-naphthalenecarbonyl)piperidin-4-yl} ß-phenoxypropionic acid, 4-{1-(2-naphthalenecarbonyl)piperidin-4-yl} γ-phenoxybutyric acid, 2-{1-(1-

naphthalenecarbonyl)piperidin-3-en-4-yl} phenoxyacetic acid, 2-{1-(1-naphthalenecarbonyl)piperidin-3-en-4-yl} ß-phenoxypropionic acid, 2-{1-(1-naphthalenecarbonyl)piperidin-3-en-4-yl} γ-phenoxybutyric acid, 3-{1-(1-naphthalenecarbonyl)piperidin-3-en-4-yl} phenoxyacetic acid, 3-{1-(1-naphthalenecarbonyl)piperidin-3-en-4-yl} ß-phenoxypropionic acid, 3-{1-(1-naphthalenecarbonyl)piperidin-3-en-4-yl} γ-phenoxybutyric acid, 4-{1-(1-naphthalenecarbonyl)piperidin-3-en-4-yl} phenoxyacetic acid, 4-{1-(1-naphthalenecarbonyl)piperidin-3-en-4-yl} ß-phenoxypropionic acid, 4-{1-(1-naphthalenecarbonyl)piperidin-3-en-4-yl} γ-phenoxybutyric acid,

[0040] 2-{1-(2-naphthalenecarbonyl)piperidin-3-en-4-yl}phenoxyacetic acid, 2-{1-(2-naphthalenecarbonyl)piperidin-3-en-4-yl} ß-phenoxypropionic acid, 2-{1-(2-naphthalenecarbonyl)piperidin-3-en-4-yl} γ-phenoxybutyric acid, 3-{1-(2-naphthalenecarbonyl)piperidin-3-en-4-yl}phenoxyacetic acid, 3-{1-(2-naphthalenecarbonyl)piperidin-3-en-4-yl} ß-phenoxypropionic acid, 3-{1-(2-naphthalenecarbonyl)piperidin-3-en-4-yl} γ-phenoxybutyric acid, 4-{1-(2-naphthalenecarbonyl)piperidin-3-en-4-yl}phenoxyacetic acid, 4-{1-(2-naphthalenecarbonyl)piperidin-3-en-4-yl} ß-phenoxypropionic acid, 4-{1-(2-naphthalenecarbonyl)piperidin-3-en-4-yl} γ-phenoxybutyric acid,

[0041] 2-{4-(2-naphthalenecarbonyl)piperazinyl) phenylacetic acid, 2-{4-(2-naphthalenecarbonyl)piperazinyl} ß-phenylpropionic acid, 2-{4-(2-naphthalenecarbonyl)piperazinyl} γ-phenylbutyric acid, 3-{4-(2-naphthalenecarbonyl)piperazinyl}phenylacetic acid, 3-{4-(2-naphthalenecarbonyl)piperazinyl} ß-phenylpropionic acid, 3-{4-(2-naphthalenecarbonyl)piperazinyl} γ-phenylbutyric acid, 4-{4-(2-naphthalenecarbonyl)piperazinyl}phenylacetic acid, 4-{4-(2-naphthalenecarbonyl)piperazinyl} ß-phenylpropionic acid, 4-{4-(2-naphthalenecarbonyl)piperazinyl} γ-phenylbutyric acid,

[0042] 2-{1-(1-naphthalenecarbonyl)piperidin-4-yl} phenylacetic acid, 2-{1-(1-naphthalenecarbonyl)piperidin-4-yl} ß-phenylpropionic acid, 2-{1-(1-naphthalenecarbonyl)piperidin-4-yl} γ-phenylbutyric acid, 3-{1-(1-naphthalenecarbonyl)piperidin-4-yl}phenylacetic acid, 3-{1-(1-

naphthalenecarbonyl)piperidin-4-yl} ß-phenylpropionic acid, 3-{1-(1-naphthalenecarbonyl)piperidin-4-yl} γ-phenylbutyric acid, 4-{1-(1-naphthalenecarbonyl)piperidin-4-yl}phenylacetic acid, 4-{1-(1-naphthalenecarbonyl)piperidin-4-yl} ß-phenylpropionic acid, 4-{1-(1-naphthalenecarbonyl)piperidin-4-yl} γ-phenylbutyric acid,

[0043] 2-{1-(2-naphthalenecarbonyl)piperidin-4-yl} phenylacetic acid, 2-{1-(2-naphthalenecarbonyl)piperidin-4-yl} ß-phenylpropionic acid, 2-{1-(2-naphthalenecarbonyl)piperidin-4-yl} γ-phenylbutyric acid, 3-{1-(2-naphthalenecarbonyl)piperidin-4-yl}phenylacetic acid, 3-{1-(2-naphthalenecarbonyl)piperidin-4-yl} ß-phenylpropionic acid, 3-{1-(2-naphthalenecarbonyl)piperidin-4-yl} γ-phenylbutyric acid, 4-{1-(2-naphthalenecarbonyl)piperidin-4-yl}phenylacetic acid, 4-{1-(2-naphthalenecarbonyl)piperidin-4-yl} ß-phenylpropionic acid, 4-{1-(2-naphthalenecarbonyl)piperidin-4-yl} γ-phenylbutyric acid, 2-{1-(1-naphthalenecarbonyl)piperidin-3-en-4-yl}phenylacetic acid, 2-{1-(1-naphthalenecarbonyl)piperidin-3-en-4-yl} ß-phenylpropionic acid, 2-{1-(1-naphthalenecarbonyl)piperidin-3-en-4-yl} γ-phenylbutyric acid, 3-{1-(1-naphthalenecarbonyl)piperidin-3-en-4-yl}phenylacetic acid, 3-{1-(1-naphthalenecarbonyl)piperidin-3-en-4-yl} ß-phenylpropionic acid, 3-{1-(1-naphthalenecarbonyl)piperidin-3-en-4-yl} γ-phenylbutyric acid, 4-{1-(1-naphthalenecarbonyl)piperidin-3-en-4-yl} phenylacetic acid, 4-{1-(1-naphthalenecarbonyl)piperidin-3-en-4-yl} ß-phenylpropionic acid, 4-{1-(1-naphthalenecarbonyl)piperidin-3-en-4-yl} γ-phenylbutyric acid,

[0044] 2-{1-(2-naphthalenecarbonyl)-4-hydroxypiperidin-4-yl}phenylacetic acid, 2-{1-(2-naphthalenecarbonyl)-4-hydroxypiperidin-4-yl} ß-phenylpropionic acid, 2-{1-(2-naphthalenecarbonyl)-4-hydroxypiperidin-4-yl} γ-phenylbutyric acid, 3-{1-(2-naphthalenecarbonyl)-4-hydroxypiperidin-4-yl}phenylacetic acid, 3-{1-(2-naphthalenecarbonyl)-4-hydroxypiperidin-4-yl} ß-phenylpropionic acid, 3-{1-(2-naphthalenecarbonyl)-4-hydroxypiperidin-4-yl} γ-phenylbutyric acid, 4-{1-(2-naphthalenecarbonyl)-4-hydroxypiperidin-4-yl}phenylacetic acid, 4-{1-(2-

naphthalenecarbonyl)-4-hydroxypiperidin-4-yl} ß-phenylpropionic acid, 4-{1-(2-naphthalenecarbonyl)-4-hydroxypiperidin-4-yl} γ-phenylbutyric acid,

[0045] 3-(4-nicotinoylpiperazinyl) phenoxyacetic acid, 3-(4-nicotinoylpiperazinyl) phenylacetic acid, 3-(1-nicotinoylpiperidin-4-yl) phenoxyacetic acid, 3-(1-nicotinoylpiperidin-4-yl) phenylacetic acid, 3-(1-nicotinoylpiperidin-3-en-4-yl) phenylacetic acid,

[0046] 3-(1-nicotinoyl-4-hydroxypiperidin-4-yl) phenoxyacetic acid, 3-(1-nicotinoyl-4-hydroxypiperidin-4-yl) phenylacetic acid,

[0047] 3-{4-(2-furancarbonyl)piperazinyl}phenoxyacetic acid, 3-{4-(2-furancarbonyl)piperazinyl} phenylacetic acid, 3-{1-(2-furancarbonyl)piperidin-4-yl} phenoxyacetic acid, 3-{1-(2-furancarbonyl)piperidin-4-yl} phenylacetic acid, 3-{1-(2-furancarbonyl)piperidin-3-en-4-yl} phenoxyacetic acid, 3-{1-(2-furancarbonyl)-4-hydroxypiperidin-4-yl} phenoxyacetic acid, 3-{1-(2-furancarbonyl)-4-hydroxypiperidin-4-yl} phenylacetic acid, 3-{1-(2-furancarbonyl)-4-hydroxypiperidin-4-yl} α, α dimethylphenoxyacetic acid,

[0048] 3-{1-(2-furancarbonyl)piperidin-3-en-4-yl} phenylacetic acid, 3-(1-isonicotinoyl-4-hydroxypiperidin-4-yl) α, α dimethylphenoxyacetic acid,

[0049] 3-(4-tenoylpiperazinyl) phenoxyacetic acid, 3-(4-tenoylpiperazinyl) phenylacetic acid, 3-(1-tenoylpiperidin-4-yl) phenoxyacetic acid, 3-(1-tenoylpiperidin-4-yl) phenylacetic acid, 3-(1-tenoylpiperidin-3-en-4-yl) phenoxyacetic acid, 3-(1-tenoylpiperidin-3-en-4-yl) phenylacetic acid, 3-(1-tenoyl-4-hydroxypiperidin-4-yl) phenoxyacetic acid, 3-(1-tenoyl-4-hydroxypiperidin-4-yl) α, α dimethylphenoxyacetic acid, 3-(1-tenoyl-4-hydroxypiperidin-4-yl) phenylacetic acid,

[0050] 3-{4-(4-quinolincarbonyl)piperazinyl} phenoxyacetic acid, 3-{4-(4-quinolincarbonyl)piperazinyl} phenylacetic acid, 3-{1-(4-quinolincarbonyl)piperidin-4-yl} phenoxyacetic acid, 3-{1-(4-quinolincarbonyl)piperidin-4-yl} phenylacetic acid, 3-{1-(4-quinolincarbonyl)-4-hydroxypiperidin-4-yl} phenoxyacetic acid, 3-{1-(4-quinolincarbonyl)-4-hydroxypiperidin-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(4-quinolincarbonyl)-4-hydroxypiperidin-4-yl} phenylacetic acid,

[0051] 3-{4-(2-indolcarbonyl)piperazinyl} phenoxyacetic acid, 3-{1-(2-indolcarbonyl)piperidin-4-yl} phenoxyacetic acid, 3-{1-(2-indolcarbonyl)-4-

hydroxypiperidin-4-yl} phenoxyacetic acid, 3-{1-(2-indolcarbonyl)piperidin-3-en-4-yl} phenoxyacetic acid, 3-{1-(2-indolcarbonyl)-4-hydroxypiperidin-4-yl} α, α dimethylphenoxyacetic acid,

[0052] 2-{1-(3-indolcarbonyl)piperidin-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(3-indolcarbonyl)piperidin-4-yl} α, α dimethylphenoxyacetic acid, 4-{1-(3-indolcarbonyl)piperidin-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(3-indolcarbonyl)piperidin-4-yl} α, α dimethylphenoxyacetic acid isopropyl, 2-{1-(2-quinolincarbonyl)piperidin-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(2-quinolincarbonyl)piperidin-4-yl} α, α dimethylphenoxyacetic acid, 4-{1-(2-quinolincarbonyl)piperidin-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(2-quinolincarbonyl)piperidin-4-yl} α, α dimethylphenoxyacetic acid isopropyl, 2-{1-(1-naphthalenecarbonyl)piperidin-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(1-naphthalenecarbonyl)piperidin-4-yl} α, α dimethylphenoxyacetic acid, 4-{1-(1-naphthalenecarbonyl)piperidin-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(1-naphthalenecarbonyl)piperidin-4-yl} α, α dimethylphenoxyacetic acid isopropyl,

[0053] [2-{4-(3-indolcarbonyl)piperazinyl}phenoxy] α, α dimethylacetic acid, [3-{4-(3-indolcarbonyl)piperazinyl}phenoxy] α, α dimethylacetic acid, [4-{4-(3-indolcarbonyl)piperazinyl}phenoxy] α, α dimethylacetic acid, [3-{4-(3-indolcarbonyl)piperazinyl}phenoxy] α, α dimethylacetic acid isopropyl, [2-{4-(2-quinolincarbonyl)piperazinyl}phenoxy] α, α dimethylacetic acid, [3-{4-(2-quinolincarbonyl)piperazinyl}phenoxy] α, α dimethylacetic acid, [4-{4-(2-quinolincarbonyl)piperazinyl}phenoxy] α, α dimethylacetic acid, [3-{4-(2-quinolincarbonyl)piperazinyl}phenoxy] α, α dimethylacetic acid isopropyl, [2-{4-(1-naphthalenecarbonyl)piperazinyl}phenoxy] α, α dimethylacetic acid, [3-{4-(1-naphthalenecarbonyl)piperazinyl}phenoxy] α, α dimethylacetic acid, [4-{4-(1-naphthalenecarbonyl)piperazinyl}phenoxy] α, α dimethylacetic acid, [3-{4-(1-naphthalenecarbonyl)piperazinyl}phenoxy] α, α dimethylacetic acid isopropyl,

[0054] 2-{1-(3-indolcarbonyl)piperidin-3-en-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(3-indolcarbonyl)piperidin-3-en-4-yl} α, α dimethylphenoxyacetic acid, 4-{1-(3-

indolcarbonyl)piperidin-3-en-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(3-indolcarbonyl)piperidin-3-en-4-yl} α, α dimethylphenoxyacetic acid isopropyl, 2-{1-(2-quinolincarbonyl)piperidin-3-en-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(2-quinolincarbonyl)piperidin-3-en-4-yl} α, α dimethylphenoxyacetic acid, 4-{1-(2-quinolincarbonyl)piperidin-3-en-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(2-quinolincarbonyl)piperidin-3-en-4-yl} α, α dimethylphenoxyacetic acid isopropyl, ***2-{1-(1-napthalenecarbonyl)piperidin-3-en-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(1-napthalenecarbonyl)piperidin-3-en-4-yl} α, α dimethylphenoxyacetic acid, 4-{1-(1-napthalenecarbonyl)piperidin-3-en-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(1-napthalenecarbonyl)piperidin-3-en-4-yl} α, α dimethylphenoxyacetic acid isopropyl,

[0055] 2-{1-(2,4-difluorobenzoyl)piperidin-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(2,4-difluorobenzoyl)piperidin-4-yl} α, α dimethylphenoxyacetic acid, 4-{1-(2,4-difluorobenzoyl)piperidin-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(2,4-difluorobenzoyl)piperidin-4-yl} α, α dimethylphenoxyacetic acid isopropyl, [2-{4-(2,4-difluorobenzoyl)piperazinyl}phenoxy] α, α dimethylacetic acid, [3-{4-(2,4-difluorobenzoyl)piperazinyl}phenoxy] α, α dimethylacetic acid, [4-{4-(2,4-difluorobenzoyl)piperazinyl}phenoxy] α, α dimethylacetic acid, [3-{4-(2,4-difluorobenzoyl)piperazinyl}phenoxy] α, α dimethylacetic acid isopropyl, 2-{1-(2,4-difluorobenzoyl)piperidin-3-en-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(2,4-difluorobenzoyl)piperidin-3-en-4-yl} α, α dimethylphenoxyacetic acid, 4-{1-(2,4-difluorobenzoyl)piperidin-3-en-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(2,4-difluorobenzoyl)piperidin-3-en-4-yl} α, α dimethylphenoxyacetic acid isopropyl, 2-{1-(2,4-difluorobenzoyl)-4-hydroxypiperidin-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(2,4-difluorobenzoyl)-4-hydroxypiperidin-4-yl} α, α dimethylphenoxyacetic acid, 4-{1-(2,4-difluorobenzoyl)-4-hydroxypiperidin-4-yl} α, α dimethylphenoxyacetic acid, 3-{1-(2,4-difluorobenzoyl)-4-hydroxypiperidin-4-yl} α, α dimethylphenoxyacetic acid isopropyl.

[0056] Of these, the following are particularly preferable: 2-[3-[1-(4-methoxybenzoyl) piperidin-4-yl]phenoxy]-2-methylpropionic acid, 2-[3-[1-(4-fluorobenzoyl) piperidin-4-

yl]phenoxy]-2-methylpropionic acid, 2-[3-[1-(4-fluorobenzoyl) piperidin-4-yl]phenoxy]-2-methylpropionic acid isopropyl, 2-[3-[1-(4-chlorobenzoyl) piperidin-4-yl]phenoxy]-2-methylpropionic acid, 2-[3-[1-(4-iodobenzoyl) piperidin-4-yl]phenoxy]-2-methylpropionic acid, 2-[3-[1-(4-trifluorobenzoyl) piperidin-4-yl]phenoxy]-2-methylpropionic acid, 2-[3-[1-(3,5-di-t-butyl-4-hydroxybenzoyl) piperidin-4-yl]phenoxy]-2-methylpropionic acid and 2-[3-[1-(nicotinoyl) piperidin-4-yl]phenoxy]-2-methylpropionic acid.

[0057] The arylamide derivative (1) according to the invention can be produced by a method based on that described in JP 2952551 (B).

[0058] When as in the Example 1 below, insulin non-dependent spontaneous diabetes mellitus model mice (KK-A^y mice) consume the arylamide derivative (1) according to the invention, it shows excellent hypoglycaemic actions. Therefore, the hypoglycaemic agent according to the invention is useful as a drug for the prevention and therapy of diabetes mellitus and obesity in mammals including humans. At the same time, the arylamide derivative (1) according to the invention is a compound with ameliorative actions for severe and moderate hyperlipidaemia, including reduction in blood triglycerides, and this lipid reduction is also noted in KK-A^y mice. Today's diabetes mellitus patients often have complicating hypertension and hyperlipidaemia, and it is considered important not only to reduce blood glucose levels but also to treat these complications, particularly hyperlipidaemia. In this context, the discovery of the hypoglycaemic actions of the compounds according to the invention, which already have known hypolipidaemic actions, will be of particular utility for diabetes mellitus patients with such complications.

[0059] The dosage of the hypoglycaemic agent according to the invention varies according to the patient's weight, age, sex, method of administration, underlying health status and illness, but a dose of 1 ~1000mg per day of arylamide derivative (1) or a salt thereof is suitable when given orally and 1~100mg per day when given non-orally.

[0060] The hypoglycaemic is used as a pharmaceutical preparation, prepared by conventional methods in a variety of forms, including tablets, granules, hard capsules, soft capsules, powder, fine powders, pills, emulsions, suspensions, injectable preparations, suppositories, drip infusions and syrups.

[0061] Solid preparation such as tablets, granules, capsules etc, can be prepared using conventional methods in which appropriate additives are added to the arylamide derivative (1). When necessary, the tablets etc may be coated with sugar, gelatine, enteric or film coating etc using a suitable coating base. Additives may include, for example, lactose, sucrose, mannitol, cornstarch, synthetic or natural gum, crystal cellulose or other excipients, starch, cellulose derivatives, gum Arabic, gelatine, polyvinyl pyrrolidone or other binder, carboxymethyl cellulose calcium, carboxymethyl cellulose sodium, starch, cornstarch, sodium alginate or other disintegrants and talc, magnesium stearate, sodium stearate or other lubricants and, when necessary, sweeteners, colouring agents, bulking agents etc may optionally be added.

[0062] When the agent is a suspension, emulsion, syrup etc, this may be prepared by dissolving or suspending an arylamide derivative (1) according to the invention in sterile water or other generally used solvent and adding, when necessary, an appropriate wetting agent, emulsifier, dispersion aid, surfactant, sweetener, perfume and/or colouring agent

[0063] When the agent is used as an injectable preparation, an arylamide derivative (1) according to the invention is first dissolved, suspended or emulsified in injectable distilled water or other aqueous carrier or is prepared as a powder for injection and dissolved etc at the time of use. Methods of administering this injectable preparation include intravenous administration, intraportal injection, intraperitoneal administration, intramuscular administration and subcutaneous administration.

[0064]

[Examples] Next the present invention is described in greater detail through examples.

[0065] Example 1

(1) Animals used

8-week-old KK-A^y male mice (insulin non-dependent spontaneous diabetes mellitus model mice; Nihon Kurea) were kept beforehand for 2 weeks, then their blood glucose (nonfasting) was measured using a Mediace Blood Glucose Measurement Reader GR-100 (Terumo) and then divided into groups (of 8 animals each) with approximately the same blood glucose values (390mg/dl or greater) and weight (35g or heavier).

[0066] (2) Drug used

2-[3-[1-(4-fluorobenzoyl) piperidin-4-yl]phenoxy]-2-methylpropionic acid (Compound 1) was synthesised by a method based on that described in JP 2952551 (B) and, as a comparison, bezafibrate(2-[4-[2-[(4-chlorobenzoyl)amino]ethyl] phenoxy]-2-methylpropionic acid), a fibrate agent for the treatment of hyperlipidaemia, was used. The said compound (0.003, 0.01, or 0.03%) or bezafibrate (0.03, 0.1, or 0.3%) was added to a powdered feed (MF) to prepare a mixed feed. Calculation of the dosage from the quantity eaten indicated that, at 0.003, 0.01, or 0.03%, this was 4.5, 14.0 and 41.2mg/kg/day of the compound and 45.1, 143.0 and 376.6mg/kg day of bezafibrate.

[0067] (3) Reagents

Glucose B test Wako (Wako Pure Chemicals), HDL-cholesterol sedimentation reagent set (Wako Pure Chemicals), triglyceride E-test Wako (Wako Pure Chemicals) and cholesterol E test Wako (Wako Pure Chemicals) were used as serum biochemical value assay reagents.

[0068] (4)Methods

The KK-A^y male mice were allowed to eat the mixed feed *ad libitum* for 14 days and hen a blood sample was taken (by cervical incision) and the serum separated (by centrifugation at 3000 rpm for 15 minutes). Serum glucose, HDL cholesterol (HDL-C) and triglycerides (TG) were then measured.

[0069] (5) Statistical tests

The test results were measured as mean values ±standard error, subjected to Bartlett's test, and then to Dunnets's test, either parametric or nonparametric, with $p<0.05$ as a significant difference (two-sided test). The results are shown in Table 1.

[0070]

[Table 1]

		Dose (mg/kg/day)	Glucose (mg/dL)	HDL-C (mg/dL)	TG (Mg/dL)
Control		-	551.6±15.3	102.5±5.7	869±65.1
Compound 1 according to the invention	0.003%	4.5±0.0	469.7±34.9 (14.8)	148.8±4.9** (45.2)	708.3±72.2 (18.5)
	0.01%	14.0±0.1	398.4±23.8** (87.8)	148.6±6.4** (45.0)	536.0±29.1** (30.3)
	0.03%	41.2±0.6	414.7±31.6** (24.8)	150.0±3.9** (46.3)	594.0±52.7** (31.6)
Bezafibrate	0.03%	45.1±0.5	496.0±39.5 (10.1)	125.2±6.8* (22.1)	746.9±83.1 (14.0)
	0.1%	143.0±1.3	440.7±22.7* (20.1)	135.6±1.9** (32.3)	661.0±24.8 (13.9)
	0.3%	376.6±4.3	258.1±18.6** (53.2)	105.1±3.9 (2.5)	451.4±18.4** (48.0)

* : $p<0.05$
** : $p<0.01$

[0071] The blood glucose values show that there was significant decrease (27.8%) with Compound 1 according to the invention and bezafibrate showed a dose-dependent lowering action, 0.1 showing a significant lowering (20.1%). For the HDL-C values, Compound 1 according to the present invention showed a significant increase (45.2%) at 0.003% and bezafibrate showed a significant increase (22.1%) at 0.03%. For the TG values, there was a significant decrease (38.3%) with Compound 1 according to the invention at 0.01% and bezafibrate showed a dose-dependent lowering action and significant decrease (48.0%) at 0.3%. The said compound according to the invention showed a titre at least 10-fold that of the bezafibrate comparison drug. KK-A^y mice are mice that spontaneously develop insulin non-dependent diabetes mellitus accompanied by obesity and which show hyperglycaemia and hyperlipidaemia and, since the compound according to the invention achieves significant reductions in blood glucose and TG values in these mice and also a significant elevation in HDL-C values, it is particularly useful for diabetes mellitus patients who have complicating hyperlipidaemia.

[0072] Example 2 Safety

Although Compound 1 was given orally to the mice at a dose of 300mg/kg, there were no fatalities and therefore it is safe.

[0073] Example 3 Preparations

(1) Tablets

Powders of 100mg of Compound 1, 50mg of crystalline cellulose, 50mg of lactose, 18mg of hydroxypropyl cellulose and 2mg of magnesium stearate were mixed together and pressed in a tablet press to form tablets of 220mg each.

[0074] (2) capsules

Powders of 50mg of Compound 1, 5mg of light anhydrous silicic acid, 100mg of lactose, 70mg of starch and 25mg of talc were mixed, and 250mg of this mixed powder was packed into each gelatine capsule to obtain capsule preparations.

[0075]

[Effects of the invention] Since the hypoglycaemic agent according to the invention has excellent hypoglycaemic actions it may be used to prevent and treat diabetes mellitus and obesity and, in particular, it may be used to prevent and inhibit the progress of atherosclerosis in diabetes mellitus patients who also have the complications of lipid metabolism abnormalities such as lowered HDL-C and elevated TG. It is thus of great clinical utility.

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